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Appl. No. 09/724,569  
Amtd. dated April 5, 2005  
Reply to Office Action of December 29, 2005

APR 05 2005

PATENTAmendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

56. (Currently Amended) An isolated nucleic acid, comprising a sequence of nucleotides that encodes a  $\beta$ -secretase protein beginning at residue 46 and extending to position 452 of SEQ ID NO:2 or up to several amino acids beyond but lacking a transmembrane region that is at least 95% identical to a protein selected from the group consisting of SEQ ID NO: 66, SEQ ID NO: 43, SEQ ID NO: 57, SEQ ID NO: 74, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 75, and SEQ ID NO: 71, or a complementary sequence of any of such nucleotides, and specifically excluding a nucleic acid encoding a protein having the sequence SEQ ID NO: 2.

57-59. (Cancel)

60. (Withdrawn) The isolated nucleic acid of claim 56, wherein said sequence of nucleotides encodes a protease having the sequence SEQ ID NO: 74.

61. (Original) A expression vector, comprising

the isolated nucleic acid of claim 56, and

operably linked to said nucleic acid, regulatory sequences effective for expression of the nucleic acid in a selected host cell.

62. (Original) The recombinant expression vector of claim 61, wherein said vector is suitable for transfection of a bacterial cell.

63. (Currently Amended) A heterologous cell transfected with the a vector of claim 61, comprising a nucleic acid operably linked to regulatory sequences effective for

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expression of the nucleic acid in the selected host cell, wherein the nucleic acid is expressed as wherein said cell expresses a biologically active  $\beta$ -secretase beginning at residue 46 and ending at position 452 or up to several amino acids beyond position 452 of SEQ ID NO:2 but lacking a transmembrane region.

64. (Original) The cell of claim 63, wherein said cell is a eukaryotic cell.
65. (Original) The cell of claim 63, wherein said cell is a bacterial cell.
66. (Original) The cell of claim 63, wherein said cell is an insect cell.
67. (Original) The cell of claim 63, wherein said cell is a yeast cell.
68. (Original) A method of producing a recombinant  $\beta$ -secretase enzyme, comprising culturing a cell according to claim 63 under conditions to promote growth of said cell, and subjecting an extract or cultured medium from said cell to an affinity matrix.
69. (Original) The method of claim 68, wherein said affinity matrix contains a  $\beta$ -secretase inhibitor molecule.
70. (Previously Presented) The method of claim 69, wherein said inhibitor molecule is SEQ ID NO: 72.
71. (Original) The method of claim 68, wherein said matrix contains an antibody characterized by an ability to bind  $\beta$ -secretase.
72. (Currently Amended) The method of claim 71, wherein said antibody is according to claim 55 reactive with a protein selected from the group consisting of SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68 SEQ ID NO: 69, SEQ ID NO: 70 and SEQ ID NO: 74..
73. (Currently Amended) A heterologous cell, comprising

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(i) a nucleic acid molecule, operably linked to a regulatory sequence, whereby the nucleic acid is expressed as encoding an active β-secretase protein according to claim 55 beginning at residue 46 and ending at position 452 or up to several amino acids beyond position 452 of SEQ ID NO:2 but lacking a transmembrane region

(ii) a nucleic acid molecule operably linked to a regulatory sequence, whereby the nucleic acid molecule is expressed as encoding a β-secretase substrate molecule; and

(iii) operatively linked to (i) and (ii), a regulatory sequence effective for expression of said nucleic acid molecules in said cell.

74. (Original) The cell of claim 73, wherein said nucleic acid encoding said β-secretase protein is heterologous to said cell.

75. (Original) The cell of claim 73, wherein both said nucleic acids encoding said β-secretase protein encoding said β-secretase substrate molecule are heterologous to said cell.

76. (Original) The cell of claim 73, wherein said β-secretase substrate molecule is selected from the group consisting of MBP-C125wt, MBP-C125sw, APPwt, APPsw, and β-secretase cleavable fragments thereof.

77. (Original) The cell of claim 76, wherein said β-secretase-cleavable fragment has a sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96.

Claims 78-131. (Canceled)